specification.

An appropriate reference to the priority benefits to which applicants are entitled has been inserted at the appropriate location in the specification.

Applicants have carefully reviewed each of the matters raised by the Examiner in her §112, 1st paragraph, rejection and have sought to amend the specification so that it is written in "full, clear, concise, and exact terms." It is deemed that applicants have overcome this rejection and, accordingly, its withdrawal is respectfully solicited.

The Examiner's rejection of the claims under §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention is deemed to have been overcome. It is respectfully submitted that claims 21-33, inclusive, serve to overcome any claim indefiniteness as pointed out by the Examiner, and, accordingly, withdrawal of the rejection is respectfully solicited.

The claims and the application stand rejected under §103(a) as being unpatentable over Georgi et al., WO 98/34949. This rejection is respectfully traversed.

It is respectfully submitted that since in new claim 21, "possibly" is not recited as it was in former claim 1, new claim 21 serves to distinguish over the Georgi et al. reference. In similar fashion, the definition of "piperazinyl" which in former claim 4, appeared at page 40, line 24, is not recited in new claim 24. Also, the piperazinyl compound recited at xvii in former claim 5, is not recited in new claim 25. Accordingly, claims 24 and 25 also distinguish over the reference. Thus, the claimed invention is limited to those instances wherein the piperazinyl-moiety, when present, is always a substituted piperazinyl.

The substituted piperazinyl compounds of the present invention would not have been obvious to one of ordinary skill in the art from what is taught, disclosed or suggested in the Georgi et al. reference. Furthermore, the unexpectedly improved activity of the claimed compounds as shown by the test results in the specification, could not have been predicted by one of ordinary skill in the art based on the prior state of the art. Accordingly, since the claims distinguish over the reference, the Examiner has failed to establish a *prima facie* case of obviousness. The rejection under §103(a) has, accordingly, been overcome and should be

withdrawn.

In view of the amendments made to the claims the non-statutory double patenting rejection has also been overcome. Accordingly, its withdrawal is solicited.

Applicants respectfully request the issuance of a Notice of Allowance.

Attached is a Marked-Up Version of the specification.

Please charge any fees which may be due and which have not been submitted herewith to our deposit account No. 01-0035.

Respectfully submitted,

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Docket No.: 205,010

MARKED-UP VERSION SHOWING CHANGES MADE BY AMENDMENT

IN THE SPECIFICATION

Page 1, lines 22-27:

-(CH_2) - Ar_1 where r ~~=~~ is 0, 1~~/~~or 2 and Ar is an aromatic group chosen among benzene, naphthalene, thiophene, benzothiophene, pyridine, quinoline, indole, furan, benzofuran, thiazole, benzothiazole, imidazole, benzoimidazole, possibly substituted with up to 2 substituents chosen among C_{1-3} alkyl, C_{1-3} haloalkyl, ~~halo C_{1-3} alkyl~~ C_{1-3} alkyloxy~~,~~ and C_{2-4} amino-alkyloxy, halogens, OH, NH_2, CN, ~~and~~ NR_6R_7, where R_6 and R_7, are the same or different, and are H or C_{1-3} alkyl.

Page 1, lines 29-32 to page 1a, line 2:

-$(CH_2)_r$ - Ar_1 where r ~~=~~ is 0, 1~~/~~or 2 and Ar_1 is an aromatic group chosen among ~~selected from the group consisting of~~: benzene, naphthalene, ~~naphtalene~~ thiopene, benzothiopene, pyridine, quinoline, indole, furan, benzofuran, thiazole, benzothiazole, imidazole, benzoimidazole, ~~possibly~~ substituted with up to 2 groups chosen among ~~selected from the group consisting of~~: C_{1-3} alkyl, halo ~~C_{1-3} alkyl~~ C_{1-3}-haloalkyl, C_{1-3} alkyloxy~~,~~ and C_{2-4} amino-alkyloxy, halogens, OH, NH_2, CN, NR_6R_7, where R_6 and R_7 are the same or different, and are H or C_{1-3} alkyl,

Page 2, lines 10-12

or R_8 and R_9 together with the N atom to which they are linked to form a piperazine possibly substituted ~~on~~ at one of its nitrogen atoms by C_{1-3} alkyl, C_{1-3} acyl or methanesulfonyl;

Page 3, lines 10-14

In WO9834949 it is described how compounds having lower molecular weight, ~~monocyclic~~ monocyclic, containing only four bi-functional residues linked among each other by a peptide or pseudopeptide bond present pharmacological activity similar or higher than that of known compounds and moreover show a high selectivity for the human NK2 receptor.

Page 5, line 5 delete "triptophane" insert --tryptophane--.

More preferred are the compounds of formula (1) wherein:

-X_1, X_2, X_3, X_4 are -CONR-,

-R is H;

-R_1 is the lateral chain of ~~triptophane~~ tryptophane;

-R_2 is the lateral chain of phenylalanine ~~possibly~~ substituted with up to two residues ~~chosen among~~ selected from the group consisting of: chlorine, fluorine, CF_3, OH, and CN; or a group 3-pyridyl-methyl, or 4-pyridyl-methyl;

-R_3 is benzyl,~~.~~

and the other substituents are as above defined.

Page 5, lines 15-20

R_9 is a group chosen among: 4-tetrahydropyranyl, 4-tetraiodrothiopyranyl, 1-oxotetraiodrothiopyran-4-yl, 1,1 dioxo-tetrahydrothiopyran-4-yl, N-methyl-4-piperidinyl, ~~N-methansulfonyl~~N-methanesulfonyl-4-piperidinyl, N-aminosulfonyl-4-piperdinyl, or R_8 and R_9 together with the N atom to which they are linked represent N-methyl-piperazinyl, N-acetyl-piperazinyl, piperazinyl, N-methanesulfonyl-piperazinyl.

Page 10, line 32 and page 11, line 1

As starting compound the cyclo ~~{-Sue~~ {Succinic[1-(R)-amino]-Trp-Phe-[(R)-NH-$CH(CH_2C_6H_5)$-CH_2-NH]-} (Compound A).